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July 8, 2021

VIA ELECTRONIC FILING
The Honorable Colm F. Connolly
United States District Judge
J. Caleb Boggs Federal Building
844 N. King Street
Wilmington, DE 19801-3555

Re: *Par Pharm., Inc. v. Eagle Pharm., Inc.*, C.A. No. 18-823-CFC-JLH

Dear Judge Connolly:

We represent the Defendant Eagle Pharmaceuticals, Inc. ("Eagle") in the above-captioned action. Pursuant to the Court's requests during yesterday's trial, Eagle provides the following definitions for the terms identified by the Court as well as the below description of the format of an Abbreviated New Drug Application ("ANDA").

I. DEFINITIONS

The definitions of "specification" and "acceptance criteria" are codified in the Code of Federal Regulations:

- **Specification:** The "quality standard (*i.e.*, tests, analytical procedures, and acceptance criteria) provided in an approved NDA or ANDA to confirm the quality of drug substances, drug products . . . and other materials used in the production of a drug substance or drug product. For the purpose of this definition, acceptance criteria means numerical limits, ranges, or other criteria for the tests described."[1]

- **Acceptance Criteria:** The "product specifications and acceptance/rejection criteria, such as acceptable quality level and unacceptable quality level, with an associated sampling plan, that are

[1] 21 C.F.R. § 314.3(b).

> necessary for making a decision to accept or reject a lot or batch (or any other convenient subgroups of manufactured units)."[2]

The definitions of "release specification," "stability specification," "in-process specifications" and "overage" are discussed in FDA Guidance documents as set forth below. An FDA Guidance represents the FDA's "current thinking on a topic."[3] Although FDA Guidance documents are not binding, FDA uses the definitions provided therein to interpret the Federal Food, Drug, and Cosmetic Act ("FDCA") and its implementation of regulations.[4]

- **Release Specification:** Release specifications are defined as "[t]he combination of physical, chemical, biological, and microbiological tests and acceptance criteria that determine the suitability of a drug product at the time of its release."[5] Release testing, which is performed to evaluate compliance with the release specification, is governed by FDA regulations.[6]

- **Stability Specification (also called "Shelf-Life"):** Shelf-life specifications are "[t]he combination of physical, chemical, biological, and microbiological tests and acceptance criteria that determine the suitability of a drug substance throughout its retest period, or that a drug product should meet throughout its shelf life."[7] Stability testing, which is performed to evaluate compliance with the stability specification, is governed by FDA regulations.[8]

- **In-Process Specification:** The FDA's regulations provides "two principles to follow when establishing in-process specifications."[9] The first is that "in-process specifications for such characteristics [of in-

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2 21 C.F.R. § 210.3(b)(20).

3 *See, e.g.*, FDA, *Guidance for Industry: ANDA Submissions – Content and Format* 1 (2019), https://www.fda.gov/media/128127/download.

4 21 C.F.R. § 10.115(d)(3); 21 C.F.R. § 10.115(b)(1) ("Guidance documents are documents prepared for FDA staff, applicants/sponsors, and the public that describe the agency's interpretation of or policy on a regulatory issue.").

5 FDA, *Guidance for Industry: Q1A(R2) Stability Testing of New Drug Substances & Products* 19 (2003), https://www.fda.gov/media/71707/download.

6 21 C.F.R. § 211.165.

7 FDA, *supra* n.5, at 20.

8 21 C.F.R. §§ 211.166–.167, .170.

9 FDA, *Guidance for Industry: Process Validation: General Principles & Practices* 6 (2011), https://www.fda.gov/files/drugs/published/Process-Validation--General-Principles-and-Practices.pdf.

> process material and the drug product] shall be consistent with drug product final specifications. Accordingly, in-process material should be controlled to assure that the final product will meet its quality requirements."[10] The second is that "in-process specifications . . . 'shall be derived from previous acceptable process average and process variability estimates where possible and determined by the application of suitable statistical procedures where appropriate.' This requirement, in part, establishes the need for manufacturers to analyze process performance and control batch-to-batch variability."[11]
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> - **Overage:** An "[o]verage is an amount of a drug substance in excess of the label claim. The use of an overage to compensate for degradation during manufacture or a product's shelf life, or to extend the shelf life is generally discouraged."[12]

Finally, "compounding pH" is not defined by FDA. "Compounding" is "the process of combining, mixing, or altering ingredients to create a medication[.]" "Target pH" is also not defined by FDA. However, "target" is generally the desired parameter within an acceptance criteria.

II. FORM OF THE ANDA SPECIFICATION

The FDA requires a specific format for an ANDA submission. As part of that template, the FDA dedicates a particular "module," Module 3, to Quality.[13] Module 3 requires the submission of both release specifications and stability specifications, but they are submitted in different sections of Module 3. Specifically, Section 3.2.*S*.7 contains all drug *substance* (*e.g.*, vasopressin API) stability data, and Section 3.2.*P*.8 contains all drug *product* (*e.g.*, an injectable vasopressin product) stability data, including "any analytical procedures and testing schedules for maintenance of the microbial product quality" and all stability protocols.[14] Conversely, drug-substance-control specifications, including "the tests, acceptance criteria, and references to methods" are submitted in Section 3.2.S.4, and drug-product-control specifications are submitted in Section 3.2.P.5.[15]

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[10] *Id.* (alteration in original).
[11] *Id.* (alteration in original).
[12] FDA, *Guidance for Industry: Allowable Excess Volume & Labeled Vial Fill Size in Injectable* 2 n.7 (2015), https://www.fda.gov/media/88138/download.
[13] FDA, *supra* n.3, at 15.
[14] *Id.* at 21, 26–27.
[15] *Id.* at 17, 24–25.

Respectfully,

/s/ David E. Moore

David E. Moore

DEM:nmt/7290427/45185

cc: Clerk of the Court (via hand delivery)
Counsel of Record (via electronic mail)